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NEWS 16 Aug 08 CANCERLIT reload  
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN  
NEWS 18 Aug 08 NTIS has been reloaded and enhanced  
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)  
now available on STN  
NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded  
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded  
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced  
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced  
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file  
NEWS 25 Sep 16 CA Section Thesaurus available in CAPLUS and CA  
NEWS 26 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985  
NEWS 27 Oct 21 EVENTLINE has been reloaded  
NEWS 28 Oct 24 BEILSTEIN adds new search fields  
NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN  
NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002  
NEWS 31 Nov 18 DKILIT has been renamed APOLLIT  
NEWS 32 Nov 25 More calculated properties added to REGISTRY  
NEWS 33 Dec 02 TIBKAT will be removed from STN  
NEWS 34 Dec 04 CSA files on STN  
NEWS 35 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date  
NEWS 36 Dec 17 TOXCENTER enhanced with additional content  
NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN  
NEWS 38 Dec 30 ISMEC no longer available  
NEWS 39 Jan 13 Indexing added to some pre-1967 records in CA/CAPLUS  
NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003  
NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003  
NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,  
ENERGY, INSPEC

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,  
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002

NEWS HOURS STN Operating Hours Plus Help Desk Availability

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NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
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STRUCTURE FILE UPDATES: 2 FEB 2003 HIGHEST RN 484639-64-7  
DICTIONARY FILE UPDATES: 2 FEB 2003 HIGHEST RN 484639-64-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

```
=> e monoterpene?
E1          30      MONOTERPEN/BI
E2          25      MONOTERPENE/BI
E3          0  --> MONOTERPENE?/BI
E4          1      MONOTERPENES/BI
E5          1      MONOTERPENOID/BI
E6          7      MONOTERPENOL/BI
E7          1      MONOTERPENOLS/BI
E8          1      MONOTERPENYL/BI
E9          2      MONOTES/BI
E10         2      MONOTESONE/BI
E11         53      MONOTETRA/BI
E12         2      MONOTETRABROMO/BI
```

=> s e1 or e2 or r4

30 MONOTERPEN/BI  
25 MONOTERPENE/BI  
148 R4

L1 178 MONOTERPEN/BI OR MONOTERPENE/BI OR R4

=> e monoterpen

E1 2 MONOTERPHTHALOYLHYDRAZONE/BI  
E2 30 MONOTERPEN/BI  
E3 25 --> MONOTERPENE/BI  
E4 1 MONOTERPENES/BI  
E5 1 MONOTERPENOID/BI  
E6 7 MONOTERPENOL/BI  
E7 1 MONOTERPENOLS/BI  
E8 1 MONOTERPENYL/BI  
E9 2 MONOTES/BI  
E10 2 MONOTESONE/BI  
E11 53 MONOTETRA/BI  
E12 2 MONOTETRABROMO/BI

=> s e2 or e3 or e4

30 MONOTERPEN/BI  
25 MONOTERPENE/BI  
1 MONOTERPENES/BI

L2 30 MONOTERPEN/BI OR MONOTERPENE/BI OR MONOTERPENES/BI

=> e sesquiterpene?

E1 52 SESQUITERPEN/BI  
E2 48 SESQUITERPENE/BI  
E3 0 --> SESQUITERPENE?/BI  
E4 4 SESQUITERPENES/BI  
E5 2 SESQUITERPENOID/BI  
E6 1 SESQUITERPENOIDAL/BI  
E7 4 SESQUITERPENOIDS/BI  
E8 1 SESQUITERPENOL/BI  
E9 1 SESQUITERPINE/BI  
E10 1 SESQUITERPINEN/BI  
E11 1 SESQUITERPINENOL/BI  
E12 1 SESQUITETRA/BI

=> s e1 or e2 or e4

52 SESQUITERPEN/BI  
48 SESQUITERPENE/BI  
4 SESQUITERPENES/BI

L3 52 SESQUITERPEN/BI OR SESQUITERPENE/BI OR SESQUITERPENES/BI

=> fil .search

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	39.58	39.79

FILE 'MEDLINE' ENTERED AT 12:16:30 ON 03 FEB 2003

FILE 'CAPLUS' ENTERED AT 12:16:30 ON 03 FEB 2003

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FILE 'BIOSIS' ENTERED AT 12:16:30 ON 03 FEB 2003

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FILE 'USPATFULL' ENTERED AT 12:16:30 ON 03 FEB 2003

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=> d his

(FILE 'HOME' ENTERED AT 12:13:36 ON 03 FEB 2003)

FILE 'REGISTRY' ENTERED AT 12:13:55 ON 03 FEB 2003  
E MONOTERPENE?

L1 178 S E1 OR E2 OR R4

E MONOTERPENE

L2 30 S E2 OR E3 OR E4

E SESQUITERPENE?

L3 52 S E1 OR E2 OR E4

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, EMBASE' ENTERED AT 12:16:30 ON  
03 FEB 2003

=> s 12 or 13

L4 1412 L2 OR L3

=> s 14 and (tumor? or tumour?)

L5 20 L4 AND (TUMOR? OR TUMOUR?)

=> dup rem 15

PROCESSING COMPLETED FOR L5

L6 18 DUP REM L5 (2 DUPLICATES REMOVED)

=> d ibib ab 1-

YOU HAVE REQUESTED DATA FROM 18 ANSWERS - CONTINUE? Y/ (N) :y

L6 ANSWER 1 OF 18 USPATFULL  
 ACCESSION NUMBER: 2002:67348 USPATFULL  
 TITLE: Sesquiterpene synthases from grand fir (*Abies grandis*).  
 INVENTOR(S): Croteau, Rodney Bruce, Pullman, WA, UNITED STATES  
 Bohlmann, Jorg, Jena, GERMANY, FEDERAL REPUBLIC OF  
 Crock, John E., Moscow, ID, UNITED STATES  
 Steele, Christopher L., Ardmore, OK, UNITED STATES  
 PATENT ASSIGNEE(S): Washington State University Research Foundation (U.S. corporation)

NUMBER	KIND	DATE
US 2002038001	A1	20020328
US 6451576	B2	20020917

APPLICATION INFO.: US 2001-865171 A1 20010524 (9)  
 RELATED APPLN. INFO.: Division of Ser. No. US 1999-234393, filed on 20 Jan 1999, GRANTED, Pat. No. US 6265639

NUMBER	DATE
US 1998-72204P	19980122 (60)

PRIORITY INFORMATION: DOCUMENT TYPE: Utility  
 FILE SEGMENT: APPLICATION  
 LEGAL REPRESENTATIVE: CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC, 1420 FIFTH AVENUE, SUITE 2800, SEATTLE, WA, 98101-2347  
 NUMBER OF CLAIMS: 29  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 4 Drawing Page(s)  
 LINE COUNT: 5307

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB cDNAs encoding E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase from Grand Fir (*Abies grandis*) have been isolated and sequenced, and the corresponding amino acid sequences have been determined. Accordingly, isolated DNA sequences

(SEQ ID No:12; SEQ ID No:19 and SEQ ID No:23) are provided which code for the expression of E.-alpha.-bisabolene synthase (SEQ ID No:13), .delta.-selinene synthase (SEQ ID No:20) and .gamma.-humulene synthase (SEQ ID No:24), respectively, from Grand Fir (*Abies grandis*). In other aspects, replicable recombinant cloning vehicles are provided which code for E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase, or for a base sequence sufficiently complementary to at least a portion of E.-alpha.-bisabolene synthase, .delta.-selinene synthase or .gamma.-humulene synthase DNA or RNA to enable hybridization therewith. In yet other aspects, modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding E.-alpha.-bisabolene synthase, .delta.-selinene synthase or .gamma.-humulene synthase. Thus, systems and methods are provided for the recombinant expression of the aforementioned recombinant sesquiterpene synthases that may be used to facilitate their production, isolation and purification in significant amounts. Recombinant

L6 ANSWER 1 OF 18 USPATFULL (Continued)  
 E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase may be used to obtain expression or enhanced expression of E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase in plants in order to enhance the production of sesquiterpenoids, or may be otherwise employed for the regulation or expression of E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase, or the production of their products.

L6 ANSWER 2 OF 18 USPATFULL  
 ACCESSION NUMBER: 2002:194743 USPATFULL  
 TITLE: Monoterpene synthases from grand fir (*Abies grandis*)  
 INVENTOR(S): Steele, C. L., Ardmore, OK, United States  
 Bohlmann, Joerg, Jena, GERMANY, FEDERAL REPUBLIC OF  
 Croteau, Rodney B., Pullman, WA, United States  
 PATENT ASSIGNEE(S): Washington State University Research Foundation, Pullman, WA, United States (U.S. corporation)

NUMBER	KIND	DATE
US 6429014	B1	20020806
US 1999-360545	19990726 (9)	

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1998-US14528, filed on 10 Jul 1998

NUMBER	DATE
US 1997-52249P	19970711 (60)

PRIORITY INFORMATION: DOCUMENT TYPE: Utility  
 FILE SEGMENT: GRANTED  
 PRIMARY EXAMINER: Bui, Phuong T.  
 LEGAL REPRESENTATIVE: Christensen O'Connor Johnson Kindness PLLC  
 NUMBER OF CLAIMS: 12  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 25 Drawing Figure(s); 25 Drawing Page(s)  
 LINE COUNT: 5595

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB cDNAs encoding gymnosperm monoterpene synthases have been isolated and sequenced, and the corresponding amino acid sequences have been determined. Modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding a monoterpene synthase of the invention. Thus, systems and methods are provided for the recombinant expression of recombinant monoterpene synthases that may be used to facilitate their production, isolation and purification in significant amounts.

L6 ANSWER 3 OF 18 USPATFULL  
 ACCESSION NUMBER: 2001:178834 USPATFULL  
 TITLE: Geranyl diphosphate synthase large subunit, and methods  
 INVENTOR(S): Croteau, Rodney B., Pullman, WA, United States  
 Burke, Charles C., Moscow, ID, United States  
 Wildung, Mark R., Colfax, WA, United States  
 PATENT ASSIGNEE(S): Washington State University Research Foundation, Pullman, WA, United States (U.S. corporation)

NUMBER	KIND	DATE
US 6303330	B1	20011016
US 1999-420211	19991018 (9)	

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1998-US21772, filed on 15 Oct 1998 Continuation-in-part of Ser. No. US 1997-951924, filed on 16 Oct 1997, now patented, Pat. No. US 5876964

DOCUMENT TYPE: Utility  
 FILE SEGMENT: GRANTED  
 PRIMARY EXAMINER: Brusca, John S.  
 LEGAL REPRESENTATIVE: Christensen O'Connor Johnson Kindness PLLC  
 NUMBER OF CLAIMS: 24  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)  
 LINE COUNT: 2145

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB A cDNA encoding geranyl diphosphate synthase large subunit from peppermint has been isolated and sequenced, and the corresponding amino acid sequence has been determined. Replicable recombinant cloning vehicles are provided which code for geranyl diphosphate synthase large subunit. In another aspect, modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding geranyl diphosphate synthase large subunit. In yet another aspect, the present invention provides isolated, recombinant geranyl diphosphate synthase protein comprising an isolated, recombinant geranyl diphosphate synthase large subunit protein and an isolated, recombinant geranyl diphosphate synthase small subunit protein. Thus, systems and methods are provided for the recombinant expression of geranyl diphosphate synthase.

## L6 ANSWER 4 OF 18 USPATFULL

ACCESSION NUMBER: 2001:17244 USPATFULL  
 TITLE: Gymnosperm nucleic acid molecules encoding  
 sesquiterpene synthases and methods of use  
 INVENTOR(S): Croteau, Rodney Bruce, Pullman, WA, United States  
 Bohmann, Jorg, Jena, Germany, Federal Republic of  
 Jetter, Reinhard, Wurzburg, Germany, Federal Republic  
 of  
 Crock, John E., Moscow, ID, United States  
 Steele, Christopher L., Admore, OK, United States  
 Washington State University Foundation, Pullman, WA,  
 United States (U.S. corporation)

NUMBER	KIND	DATE
US 6265639	B1	20010724
US 1999-234393		19990120 (9)

NUMBER	DATE
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PRIORITY INFORMATION: US 1998-72204P 19980122 (60)  
 DOCUMENT TYPE: Utility  
 FILE SEGMENT: GRANTED  
 PRIMARY EXAMINER: Nelson, Amy J.  
 LEGAL REPRESENTATIVE: Christensen O'Connor Johnson Kindness PLLC  
 NUMBER OF CLAIMS: 17  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)  
 LINE COUNT: 2543

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB CDNAs encoding E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase from Grand Fir (*Abies grandis*) have been isolated and sequenced, and the corresponding amino acid sequences have been determined. Accordingly, isolated DNA sequences (SEQ ID No:12 and SEQ ID No:19 and SEQ ID No:23) are provided which code for the expression of E.-alpha.-bisabolene synthase (SEQ ID No:13), .delta.-selinene synthase (SEQ ID No:20) and .gamma.-humulene synthase (SEQ ID No: 24), respectively, from Grand Fir (*Abies grandis*). In other aspects, replicable recombinant cloning vehicles are provided which

code for E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase, or for a base sequence sufficiently complementary to at least a portion of E.-alpha.-bisabolene synthase, .delta.-selinene synthase or .gamma.-humulene synthase DNA or RNA to enable hybridization therewith. In yet other aspects, modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding E.-alpha.-bisabolene synthase, .delta.-selinene synthase or .gamma.-humulene synthase. Thus, systems and methods are provided for the recombinant expression of the aforementioned recombinant sesquiterpene synthases that may be used to facilitate their production, isolation and purification in significant amounts. Recombinant E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase may be used to obtain expression or enhanced expression of E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase in plants, or may be otherwise employed

## L6 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:567520 BIOSIS  
 DOCUMENT NUMBER: PREV200100567520  
 TITLE: The GDNF/RET signaling pathway and human diseases.  
 AUTHOR(S): Takahashi, Masahide (1)  
 CORPORATE SOURCE: (1) Department of Pathology, Graduate School of Medicine, Nagoya University, 65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550 mtakaha@med.nagoya-u.ac.jp Japan  
 SOURCE: Cytokine & Growth Factor Reviews, (December, 2001) Vol. 12,  
 No. 4, pp. 361-373. print.  
 ISSN: 1359-6101.

DOCUMENT TYPE: General Review  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

## L6 ANSWER 4 OF 18 USPATFULL (Continued)

for the regulation or expression of E.-alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase.

## L6 ANSWER 6 OF 18 USPATFULL

ACCESSION NUMBER: 2000:70973 USPATFULL  
 TITLE: Chimeric isoprenoid synthases and uses thereof  
 INVENTOR(S): Chappell, Joseph, Lexington, KY, United States  
 Back, Kyungwhan, Lexington, KY, United States  
 PATENT ASSIGNEE(S): Board of Trustees of the University of Kentucky, Lexington, KY, United States (U.S. corporation)

NUMBER	KIND	DATE
US 6072045		20000606
US 1998-134699		19980814 (9)
RELATED APPLN. INFO.:		Continuation of Ser. No. US 1996-631341, filed on 12 Apr 1996, now patented, Pat. No. US 5824774

DOCUMENT TYPE: Utility  
 FILE SEGMENT: Granted  
 PRIMARY EXAMINER: Huff, Sheila  
 LEGAL REPRESENTATIVE: Clark & Elbing, LLP  
 NUMBER OF CLAIMS: 10  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 9 Drawing Figure(s); 9 Drawing Page(s)  
 LINE COUNT: 1337

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a chimeric isoprenoid synthase polypeptide including a first domain from a first isoprenoid synthase joined to a second domain from a second, heterologous isoprenoid synthase, whereby the chimeric isoprenoid synthase is capable of catalyzing the production of isoprenoid reaction products that are not produced in the absence of the second domain of the second, heterologous isoprenoid synthase. Also disclosed is a chimeric isoprenoid synthase polypeptide including an asymmetrically positioned homologous domain, whereby the chimeric isoprenoid synthase is capable of catalyzing the production of isoprenoid reaction products that are not produced when the domain is positioned at its naturally-occurring site in the isoprenoid synthase polypeptide.

L6 ANSWER 7 OF 18 USPATFULL  
 ACCESSION NUMBER: 199943445 USPATFULL  
 TITLE: Monoterpene synthases from common sage (Salvia officinalis)  
 INVENTOR(S): Croteau, Rodney Bruce, Pullman, WA, United States  
 Wise, Mitchell Lynn, Pullman, WA, United States  
 Katahira, Eva Joy, Pullman, WA, United States  
 Savage, Thomas Jonathan, Christchurch 5, New Zealand  
 PATENT ASSIGNEE(S): Washington State University Research Foundation, United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5891697 19990406  
 APPLICATION INFO.: US 1997-937540 19970925 (8)

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Wax, Robert A.

ASSISTANT EXAMINER: Saidha, Tekchand

LEGAL REPRESENTATIVE: Christensen O'Connor Johnson & Kindness PLLC

NUMBER OF CLAIMS: 20

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 2204

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB cDNAs encoding (+)-bornyl diphosphate synthase, 1,8-cineole synthase

and

(+)-sabinene synthase from common sage (Salvia officinalis) have been isolated and sequenced, and the corresponding amino acid sequences has been determined. Accordingly, isolated DNA sequences (SEQ ID No:1; SEQ ID No:3 and SEQ ID No:5) are provided which code for the expression of (+)-bornyl diphosphate synthase (SEQ ID No:2), 1,8-cineole synthase

(SEQ ID No:4) and (+)-sabinene synthase SEQ ID No:6), respectively, from

sage (Salvia officinalis). In other aspects, replicable recombinant cloning vehicles are provided which code for (+)-bornyl diphosphate synthase, 1,8-cineole synthase or (+)-sabinene synthase, or for a base sequence sufficiently complementary to at least a portion of (+)-bornyl diphosphate synthase, 1,8-cineole synthase or (+)-sabinene synthase DNA or RNA to enable hybridization therewith. In yet other aspects,

modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding (+)-bornyl diphosphate synthase, 1,8-cineole synthase or (+)-sabinene synthase. Thus, systems and methods are provided for

the recombinant expression of the aforementioned recombinant monoterpene synthases that may be used to facilitate their production, isolation

and purification in significant amounts. Recombinant (+)-bornyl diphosphate synthase, 1,8-cineole synthase and (+)-sabinene synthase may be used to obtain expression or enhanced expression of (+)-bornyl diphosphate synthase, 1,8-cineole synthase and (+)-sabinene synthase in plants in order to enhance the production of monoterpenoids, or may be otherwise employed for the regulation or expression of (+)-bornyl diphosphate

L6 ANSWER 7 OF 18 USPATFULL (Continued)  
 synthase, 1,8-cineole synthase and (+)-sabinene synthase, or the production of their products.

L6 ANSWER 8 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 200061921 BIOSIS

DOCUMENT NUMBER: PREV200000061921

TITLE: Molecular mechanisms of RET activation in human neoplasia.

AUTHOR(S): Santoro, M. (1); Carlomagno, F.; Melillo, R. M.; Billaud, M.; Vecchio, G.; Fusco, A.

CORPORATE SOURCE: (1) Centro di Endocrinologia ed Oncologia Sperimentale del C.N.R., Universita degli Studi di Napoli, Via S. Pensini 5, 80131, Napoli Italy

SOURCE: Journal of Endocrinological Investigation, (Nov.. 1999) Vol. 22, No. 10, pp. 811-819.

ISSN: 0391-4097.

DOCUMENT TYPE: General Review

LANGUAGE: English

L6 ANSWER 9 OF 18 USPATFULL

ACCESSION NUMBER: 1998128359 USPATFULL

TITLE: Chimeric isoprenoid synthases and uses thereof  
 INVENTOR(S): Chappell, Joseph, Lexington, KY, United States  
 Back, Kyongwhan, Lexington, KY, United States  
 PATENT ASSIGNEE(S): Board of Trustees of the University of Kentucky, Lexington, KY, United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5824774 19981020  
 APPLICATION INFO.: US 1996-631341 19960412 (8)

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Huff, Sheila

LEGAL REPRESENTATIVE: Clark & Elbing LLP

NUMBER OF CLAIMS: 18

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 9 Drawing Figure(s); 9 Drawing Page(s)

LINE COUNT: 1388

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a chimeric isoprenoid synthase polypeptide including a first domain from a first isoprenoid synthase joined to a second domain from a second, heterologous isoprenoid synthase, whereby the chimeric isoprenoid synthase is capable of catalyzing the production of isoprenoid reaction products that are not produced in the absence of

the second domain of the second, heterologous isoprenoid synthase. Also disclosed is a chimeric isoprenoid synthase polypeptide including an asymmetrically positioned homologous domain, whereby the chimeric isoprenoid synthase is capable of catalyzing the production of isoprenoid reaction products that are not produced when the domain is positioned at its naturally-occurring site in the isoprenoid synthase polypeptide.

L6 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 1996:232423 BIOSIS  
 DOCUMENT NUMBER: PREV199698796552  
 TITLE: A cDNA clone for taxadiene synthase, the diterpene cyclase  
 that catalyzed the committed step of taxol biosynthesis.  
 AUTHOR(S): Wildung, Mark R.; Croteau, Rodney (1)  
 CORPORATE SOURCE: (1) Inst. Biol. Chem., Washington State University,  
 Pullman, WA 99164-6340 USA  
 SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 16,  
 pp. 9201-9204.  
 ISSN: 0021-9258.

DOCUMENT TYPE: Article  
 LANGUAGE: English

AB The committed step of taxol (paclitaxel) biosynthesis is catalyzed by tax-4(5),11(12)-diene synthase, a diterpene cyclase responsible for transforming the ubiquitous isoprenoid intermediate geranylgeranyl diphosphate to the parent olefin with a taxane skeleton. To obtain the corresponding cDNA clone, a set of degenerate primers was constructed based on consensus sequences of related monoterpene, sesquiterpene, and diterpene cyclases. Two of these primers amplified 83-base pair fragments that were cyclase-like in sequence and that was employed as a hybridization probe to screen a cDNA library constructed from poly(A)+ RNA extracted from Pacific yew (Taxus brevifolia) stems. Twelve independent clones with insert size in excess of 2 kilobase pairs were isolated and partially sequenced. One of these cDNA isolates was functionally expressed in Escherichia coli, yielding a protein that was catalytically active in converting geranylgeranyl diphosphate to a diterpene olefin that was confirmed to be tax-4(5),11(12)-diene by combined capillary gas chromatography-mass spectrometry. The sequence specifies an open reading frame of 2586 nucleotides, and the complete deduced polypeptide, including a long presumptive plastidial targeting peptide, contains 862 amino acid residues and has a molecular weight of 98,303, compared with about 79,000 previously determined for the mature native enzyme. Sequence comparisons with monoterpene, sesquiterpene, and diterpene cyclases of plant origin indicate a significant degree of similarity between these enzymes; the taxadiene synthase most closely resembles (46% identity, 67% similarity) abietadiene synthase, a diterpene cyclase from grand fir.

L6 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1996:393156 CAPLUS  
 DOCUMENT NUMBER: 125:52091  
 TITLE: Identifying functional domains within terpene  
 cyclases

AUTHOR(S): Back, Kyungwhan; Chepelli, Joseph  
 CORPORATE SOURCE: Plant Physiology/Biochemistry/Molecular Biology  
 Program, University Kentucky, Lexington, KY,  
 40546-0091, USA  
 SOURCE: Proceedings of the National Academy of Sciences of  
 the

United States of America (1996), 93(13), 6841-6845  
 CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Cyclic terpenes and terpenoids are found throughout nature. They comprise an esp. important class of compds. from plants that mediate plant-environment interactions, and they serve as pharmaceutical agents with antimicrobial and anti-tumor activities. Mol. comparisons of several terpene cyclases, the key enzymes responsible for the

multistep cyclization of C10, C15, and C20 allylic diphosphate substrates, have revealed a striking level of sequence similarity and conservation of exon position and size within the genes. Functional domains responsible for a terminal enzymic step were identified by swapping regions approximating exons between a Nicotiana tabacum 5-epiariatolochene synthase (TEAS) gene and a Hyoscyamus nigerus veticipradiene synthase (HVS) gene and by characterization of the resulting chimeric enzymes expressed in bacteria. While exon 4 of the TEAS gene conferred specificity for the predominant reaction products of the tobacco enzyme, exon 6 of the HVS gene conferred specificity for the predominant reaction product(s) of the Hyoscyamus enzyme. Combining these two functional domains of the TEAS and HVS genes resulted in a novel enzyme capable of synthesizing reaction products reflective of both parent enzymes. The relative ratio of the TEAS and

HVS reaction products was also influenced by the source of exon 5 present in the new chimeric enzymes. The assocn. of catalytic activities with conserved but sep. exonic domains suggests a general means for generating addnl. novel terpene cyclases.

L6 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1  
 ACCESSION NUMBER: 1991:600896 CAPLUS  
 DOCUMENT NUMBER: 115:200896  
 TITLE: Carcinogenic activity of the pesticide olgin in a chronic experiment in rats  
 AUTHOR(S): Petrovskaya, O. G.; Baglei, E. A.; Reshavskaya, E. V.  
 CORPORATE SOURCE: All-Union Sci. Res. Inst. Hyg. Toxicol. Pestic.,  
 Polym. Plast., Kiev, 252127, USSR  
 SOURCE: Eksperimental'naya Onkologiya (1991), 13(4), 18-20  
 CODEN: EKSODD; ISSN: 0204-3564  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian

AB Olgin administered orally to rats at doses of 0.30 and 30 mg/kg body wt. daily for 24 mo. promoted an increase in the tumor rate, the multiplicity index, and the relative risk and a decrease in the latent period. Tumor formation was high in the mammary gland, endocrine organs, and hemogenic tissues. No significant sex differences were found. The results demonstrated that olgin is carcinogenic.

L6 ANSWER 13 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 1989:319805 BIOSIS  
 DOCUMENT NUMBER: BR37:22577  
 TITLE: ELABORATION OF FUSED GEM-DIMETHYLCYCLOPROPANE SYSTEMS VIA CYCLOPROPENE CYCLOADDITION A STEREOCOMPLEMENTARY

APPROACH:  
 AUTHOR(S): RIGBY J H; KIERKUS P C  
 CORPORATE SOURCE: DEP. CHEM., WAYNE STATE UNIV., DETROIT, MICH. 48202.  
 SOURCE: J. Am. Chem. Soc., (1989) 111 (11), 4125-4126.  
 CODEN: JACSAT. ISSN: 0002-7863.

FILE SEGMENT: BR; OLD

LANGUAGE: English

L6 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1984:434310 CAPLUS  
 DOCUMENT NUMBER: 101:34312  
 TITLE: Toxicological features of T 2 toxin and related trichothecenes  
 AUTHOR(S): Ueno, Yoshiro  
 CORPORATE SOURCE: Fac. Pharm. Sci., Tokyo Univ. Sci., Tokyo, 162, Japan  
 SOURCE: Fundamental and Applied Toxicology (1984), 4(2, Pt. 2), 124-32  
 CODEN: FAATDF; ISSN: 0272-0590  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Toxicol. characteristics of toxin T 2 (I) [21259-20-1] and related trichothecenes, mycotoxins produced by Fusarium, Trichoderma, Verrucaria, and other were investigated in regard to LD50 values, dermal toxicity, hematol. changes, and tumorigenicity. The LD50 values (mg/kg) of I in adult male mice were orally 10.5, i.p. 5.2, s.c. 2.1, and i.v. 4.2, and those of nivalenol [31481-20-4] were i.p. 4.1 and i.v. 6.3. The lethal toxicity of I and nivalenol was approx. 10 times higher than deoxynivalenol [51481-10-8]. Newborn and immature animals were much more susceptible than adults. Inhalation expts. revealed that 33 ppb I for 160-min and 140 ppb for 30-min exposure were enough to cause death in mice within several days. The dermal toxicity of I and macrocyclic trichothecenes (verrucarin A [3148-09-2] and roridin A [14729-29-4]) was significantly higher than the other trichothecenes, and the induction of edema and other dermal toxicities is caused by direct attack of the trichothecenes on the capillary vessels. No tumorigenicity of fusarenon X [23255-69-8] to dermal tissues was shown in mice.

L6 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1982:162967 CAPLUS  
 DOCUMENT NUMBER: 96:162967  
 TITLE: Structural modifications of anguidin and antitumor activities of its analogs  
 AUTHOR(S): Kaneko, T.; Schmitz, H.; Essery, J. M.; Rose, W.; Howell, H. G.; O'Herron, P. A.; Nachfolger, S.; Huitalen, J.; Bradner, W. T.; et al.  
 CORPORATE SOURCE: Bristol Lab., Div. Bristol-Myers Co., Syracuse, NY, 13201, USA  
 SOURCE: Journal of Medicinal Chemistry (1982), 25(5), 579-89  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Approx. 60 derivs. of anguidin e.g., I (R = H, ClCH<sub>2</sub>CO<sub>2</sub>) tetrahydropyranyl; R1 = Ac, H, R2 = H, acyl, were prep'd. for evaluation of antitumor activities. Positions 3,4,8,9,10, and 15 were modified, and the resulting derivs. were screened against P-388 leukemia. Introduction of the C3-oxo and C3,C8-oxo groups markedly improved the antileukemic activity, whereas epoxidin. of the C9-C10 double bond or oxidin. of the C15 position diminished its activity. Selected derivs. were further tested in the L1210, B16, Lewis lung, Colon 36, and Colon 38 tumor lines. Among these compds. 4.beta.,15-diacetoxyxirpene-3,8-dione and 4.beta.-(chloroacetoxy)-15-acetoxyxirpene-3,8-dione were most active in various tumors.

L6 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1980:70705 CAPLUS  
 DOCUMENT NUMBER: 92:70705  
 TITLE: Detection of Fusarium toxic strains  
 AUTHOR(S): Payen, J.; Lafont, P.; Parache, R. M.; Boller, F.  
 CORPORATE SOURCE: Lab. Mycol. Appl., ENSAIA, Nancy, F-54000, Fr.  
 SOURCE: Collection de Medecine Legale et de Toxicologie Medicale (1978), Volume Date 1977, 107(Mycotoxines), 111-17  
 CODEN: CMIMDW; ISSN: 0398-9119  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French  
 AB Human and mouse tumor cultures were incubated in terasaki plates with toxin T 2 (I) [21259-20-1], diacetoxyscirpenol (II) [2270-40-8], neosolaniol (III) [36519-25-2], and butenolide [497-23-4] with a view to detg. the toxicity threshold (crit. titer). At the crit. level the toxins gave an asynchronous cell fraction, consisting of rounded granular cells which detached themselves and a fraction offuse-shaped cells altered in situ. Sensitivity thresholds were for I 10, II 32, III 800, and butenolide 1800  $\mu$ g/g, resp., in the human cancer test cultures. Resp. values for the mouse cancer cultures were 64, 320, 800, and 20,000  $\mu$ g/g. For test with germinating *Lepidium sativum* seed, the resp. values were 800, 10,000, 50,000, and 250,000  $\mu$ g/g. The toxins inhibited the radicle growth with great regularity. The rapidity of the *L. sativum* tests permits its use in routine checking of foods. The 3 tests gave satisfactory results with fractionated excts. from Fusarium sp., both with fractions which contained I, II, and III, and those which were toxic for chicken embryos, and in tests with fractions free of I-III which were not toxic to chicken embryos but affected the cancer cell cultures and *L. sativum* germination.

L6 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2  
 ACCESSION NUMBER: 1973:543406 CAPLUS  
 DOCUMENT NUMBER: 79:143406  
 TITLE: Comparative toxicology of trichothec mycotoxins. Inhibition of protein synthesis in animal cells  
 AUTHOR(S): Ueno, Yoshiro; Nakajima, Michiko; Sakai, Kosei; Ishii, Kenji; Sato, Norio; Shimada, Noriko  
 CORPORATE SOURCE: Fac. Pharm. Sci., Sci. Univ. Tokyo, Tokyo, Japan  
 SOURCE: Journal of Biochemistry (Tokyo, Japan) (1973), 74(2), 285-96  
 CODEN: JOBIAO; ISSN: 0021-924X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Among 14 kinds of 12,13-epoxy-trichothec mycotoxins and related antibiotics tested, 12 inhibited the uptake of <sup>14</sup>C-labeled leucine by whole cell rabbit reticulocytes. The mycotoxins inhibited the uptake of leucine and thymidine without affecting uracil uptake in Ehrlich ascite tumor cells. Rabbit reticulocyte polyribosomes were degraded by low trichothecene concns. In concns. lower than the inhibitory concns. of puromycin and cycloheximide, the trichothecenes inhibited poly-U-dependent synthesis of polyphenylalanine in cell-free reticulocyte and rat liver systems. Fusarenon-X [23255-69-8] did not inhibit protein synthesis in whole-cell or cell-free *Escherichia coli* systems, but slightly inhibited the uptake of L amino acids in yeast (*Geotrichum candidum*). Biochem. features of trichothec mycotoxin action are discussed in relation to their chem. and toxicol. characteristics.

L6 ANSWER 18 OF 18 CAPIUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1972:94528 CAPIUS  
DOCUMENT NUMBER: 76:94528  
TITLE: Cytotoxicity of sesquiterpene lactones  
AUTHOR(S): Lee, Kuo-Hsiung; Huang, Eng-Shang; Piantadosi, Claude;  
CORPORATE SOURCE: Pagano, Joseph S.; Geissman, T. A.  
Dep. Med. Chem., Univ. North Carolina, Chapel Hill,  
NC, USA  
SOURCE: Cancer Research (1971), 31(11), 1649-54  
DOCUMENT TYPE: CODEN: CNREAB; ISSN: 0008-5472  
LANGUAGE: Journal  
English  
AB The toxicity of sesquiterpene lactones to 3 human cell lines is mainly  
due to an  $\alpha$ -methylene- $\gamma$ -lactone moiety in the sesquiterpene  
molecules such as canin (1) [24959-84-0]. The cytotoxicity tests were  
performed in a microtest plate in which different concns. of 18  
sesquiterpene lactones were simultaneously tested against 3 cell lines:  
human laryngeal carcinoma, normal human fibroblasts, and human cells  
transformed with simian virus 40. Hydrogenation of the conjugated  
 $\alpha$ -methylene- $\gamma$ -lactone systems, as in  $\alpha$ -santonin  
(481-06-1), vulgarin (3162-56-9), and deacetoxymatricarin  
(10180-88-8) led to essentially inactive compds., whereas the remaining  
sesquiterpene lactones contg. the O=C-C=CH<sub>2</sub> system inhibited the growth  
of these cells.